REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

By the present amendment, claims 58, 61, 74, 77, 133 and 134 are amended. By the present amendment claims 28-30, 54-57, 96-132, and 136 are canceled without prejudice, claims 1-27 and 31-53 having been canceled by previous amendment. By the present amendment no claims are newly added. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier. Upon entry of the present amendments, claims 58-95 and 133-135 will be pending in the application with claims 58-73, 77-132, 134 and 135 withdrawn from consideration as directed to a non-elected invention. Claims 74-76, and 133 are currently under examination.

Specification

The specification has been objected to because the first paragraph of the application, and the ADS are not consistent with respect to the claim for priority. The correct claim for priority is as stated in the ADS. Accordingly, the specification has been amended to be consistent with the ADS. Applicant believes this objection to be overcome.

Rejections Under 35 U.S.C. § 112.

Claims 74-76 are rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement, and second paragraph, as lacking enablement. Specifically, the Examiner asserts that terms such as G-protein coupled receptor, lipophilic groups, neutral or anionic Lewis bases, and amino acid radicals are not supported by the specification and therefore lack written description. The Examiner also asserts that the terms lack enablement, suggesting that it is indeterminate what part of an amino acid is to be removed to render it an amino acid radical. Applicant respectfully traverses these rejections.

With respect to the term G-protein coupled receptor, while the Applicant disagrees with the Examiner's characterization, a lacking written description and enablement, the term has been deleted from the claims. However, with respect to the remaining terms, not only are such terms well understood by those of ordinary skill in the art, the specification provides ample definition and guidance with respect to such terms.

With respect to the term "lipophilic groups," Applicant submits that such a term is well understood by those of skill in the art and is well defined in the specification. For example, the literal meaning of the term from the Latin is "fat loving." In other words, those of skill in the art understand that lipophilic groups are those groups having an affinity for oils and an fats, and not for water. As defined in paragraph 54, lipophilic is defined as follows:

> [0054] The terms "lipophilic group" and "lipophilic moiety" as used herein refer to a group, moiety or substituent that has a greater affinity for non-polar or non-aqueous environments versus polar or aqueous environments. For example, Merriam Webster's online dictionary defines "lipophilic" as "having an affinity for lipids (as fats). "Exemplary lipophilic moieties include aliphatic hydrocarbon radicals, e.g., alkyl radicals, aromatic hydrocarbon radicals, and long-chain acyl radicals; all of them have increasing lipophilicity as the number of constituent carbons increases. In general, addition of a lipophilic moiety to a particular compound will increase the compound's affinity for octanol in the standard octanol/water partition-coefficient-determination protocol; this protocol may be used to gauge a compound's relative hydrophobicity (lipophilicity) and hydrophilicity.

In the specification, in at least paragraphs 20, 23, and 27, the lipophilicity of the compounds is described, as well as the benefits which are imparted to the compounds by the lipophilic groups. Paragraph 27 also provides a brief listing of groups which are understood by the person of skill in the art to be lipophilic.

> [0020] The imidazole ring systems allow for extensive derivatization due to the presence of a second heteroatom in the ring. This feature allows one to increase lipophilicity and molecular size of the complex, characteristics that are beneficial for blood flow agents. Preliminary results in rats show

> high levels of accumulation in the heart with low levels in blood, lung and liver.
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> [0023] This tridentate class of chelates offers flexibility of the lipophilicity of the chelate by modulating the lipophilic nature of R_2. R_1 may be altered to supply a ligating anionic molecule to vary the charge of the complex, and it may also be a biologically relevant molecule.
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> [0027] This class is similar to Class II in that it is hexadentate, but it offers more flexibility as to the net charge which can be adjusted through the choice of the nonimidazole arms, R_3. R_3 can be independently altered to introduce anionic ligating groups, such as carboxylate, thiolate, or phenolic substituents. Neutral ligands, such as pyridine, may also be used as R_3. In this class, R_2 can be used to modulate lipophilicity and R_3 can be used to modulate charge. R_3 may also be used to modulate lipophilicity if used with non-coordinating groups, such as ethers, alkylaryl, or aralkyl groups. R_3 may be the same or different.

Accordingly, Applicant submits that there is ample written description of "lipophilic groups," and Applicant has provided ample guidance to the person of ordinary skill in the art as to the type of groups that are considered to be lipophilic groups.

With respect to the term "neutral or anionic Lewis bases," the Applicant submits that this term is well understood by those of skill in the art and will be immediately recognized as such. Paragraph 55 of the specification provides a thorough definition of the term:

> The terms "Lewis base" and "Lewis basic" are art-recognized and generally refer to a chemical moiety capable of donating a pair of electrons under certain reaction conditions. It may be possible to characterize a Lewis base as donating a single electron in certain complexes, depending on the identity of the Lewis base and the metal ion, but for most purposes, however, a Lewis base is best understood as a two electron donor. Examples of Lewis basic moieties include uncharged compounds such as alcohols, thiols, and amines, and charged moieties such as alkoxides, thiolates, carbanions, and a variety of other organic anions. In certain examples, a Lewis base may consist of a single atom, such as oxide (O_2^-). In certain, less common circumstances, a Lewis base or ligand may be positively charged. A Lewis base, when coordinated to a metal ion, is often referred to as a ligand. Further description of ligands relevant to the present invention is presented herein.

Thus, not only has the Applicant defined the term as one which donates a pair of electrons, the Applicant has provide a listing of functional groups that may donate electrons accordingly. The person of ordinary skill in the art is well-versed from the time of their first general chemistry class as to what Lewis bases are, and can recognize them. Furthermore, the specification goes one step further stating that illustrative Lewis basis include "uncharged compounds such as alcohols, thiols, and amines, and charged moieties such as alkoxides, thiolates, carbanions, and a variety of other organic anions…[and] [i]n certain examples, a Lewis base may consist of a single atom, such as oxide (O_2^-)." Furthermore, Lewis bases include those groups generally considered to be ligands when associated with a metal ion. Based upon the knowledge of the person of ordinary skill in the art, and the express definition and direction provided to the person as to what constitutes a Lewis base, Applicant submits that the term has written description and is fully enabled.

With respect to the term "amino acid radicals," Applicant likewise believes the term to have written description and is fully enabled. In the specification at paragraph 61, the term "amino acid" is defined as:

> The term "amino acid" is art-recognized and refers to all compounds, whether natural or synthetic, which include both an amino functionality and an acid functionality, including amino acid analogs and derivatives.

Thus, those compounds which are amino acids are readily recognized by the person of ordinary skill in the art, as being of the naturally occurring amino acids, or one of those which has been synthetically prepared. They are immediately identified as having both an amino functionality and an acid functionality. With respect to the "radical" portion of the disputed term, this is likewise readily understood by the person of ordinary skill in the art, given the present specification.

The person of ordinary skill in the art, faced with the term "amino acid radical" will readily understand that it is a radical in which the amino and acid functionalities must still be

present. Additionally it is further generally recognized that a carbon derived radical is the commonly recognized as a more stable radical then one derived from a heteroatom such as oxygen or nitrogen. For example, paragraphs 141-144, 184-187, and 322-325 provide several examples of what is meant by the term:

> [0141] In certain embodiments, the compounds of the present invention are represented by B and the attendant definitions, wherein the ammo acid radical is $-CH_2CH_2CH_2CH_2CH(NH_2)CO_2H$.
>
> [0142] In certain embodiments, the compounds of the present invention are represented by B and the attendant definitions, wherein the amino acid radical is $-CH(CO_2H)CH_2CH_2CH_2CH_2NH_2$.
>
> [0143] In certain embodiments, the compounds of the present invention are represented by B and the attendant definitions, wherein the ammo acid radical is $-CH_2CH_2CO_2H$.
>
> [0144] In certain embodiments, the compounds of the present invention are represented by B and the attendant definitions, wherein the amino acid radical is $-CH(CO_2H)(CH_2)_xCH(NH_2)CO_2H$, wherein x is an integer from 3 to 9 inclusively.

In each case of the illustrated examples, the radical continues to have amino and acid functionalities in tact. There is no ambiguity in view of the definitions and illustrative examples provided. Furthermore, Scheme 3 presents a general synthetic scheme for the preparation of mono-, di- and mixed alkylated SAACs (single amino acid chelators). It is noted that "the method may be adopted to any amino acid or amino acid analogue." Thus, not only are the amino acid radicals generally defined, synthetic pathways are presented for adapting the illustrated amino acid radical in Scheme 3 to use any amino acid radical.

In view of the above remarks, Applicant submits that the terms "lipophilic groups," "neutral or anionic Lewis bases," and "amino acid radicals" are well understood by those of skill in the art, and with the definitions and examples provided, the person of ordinary skill in the art has before them in the application a road map to practice and understand the full scope of the presently claimed invention.

Rejection Under 35 U.S.C. § 102.

Claims 74-76 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 2,863,874, as issued to Gregory. Applicant respectfully traverses this rejection.

Claim 74 has been amended to recite where X is either NR^2 or O. Such imidazoles or oxazoles are not taught or suggested by Gregory. Accordingly, Applicant believes the grounds for this rejection have been successfully overcome, and requests its withdrawal.

Rejoinder

In Applicant's response to the Restriction Requirement mailed on March 23, 2010, Applicant elected Group III, encompassing 58-95 and 133. Because of the outstanding rejections have now been overcome, Applicant requests that the remaining species of Group III be examined, and that all claims of the elected group be allowed to proceed to issuance together. Accordingly, Applicant requests that claims 58-73, 77-95, 134 and 135 be rejoined to the application at the present time.

Applicants believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date February 7, 2011

By */Jeffrey R. Lomprey/*

FOLEY & LARDNER LLP
Customer Number: 48329
Telephone: (608) 258-4288
Facsimile: (608) 258-4258

Jeffrey R. Lomprey
Attorney for Applicant
Registration No. 55,401